Obesity is a complex and escalating metabolic disorder characterized by a positive disequilibrium between energy intake and energy expenditure. The consequent expansion of the adipose organ, and in particular of visceral fat depots, increases the risk of developing obesity complications such as insulin resistance, type 2 diabetes, atherosclerosis, obstructive sleep apnea, steatohepatitis, and cardio- and cerebrovascular diseases. In this context, several clinical and biochemical elements may act as risk factors for cardiovascular disease, including high-density lipoprotein cholesterol, triglycerides, increased concentrations of apolipoprotein B, and small, dense low-density lipoprotein particles, arterial hypertension, hyperglycemia, hyperuricemia, and microalbuminuria. The more risk factors are present in any individual, the higher the risk of transition to diabetes and/or cardiovascular disease (10). The increase in abdominal circumference is the clinical parameter that probably best identifies the risk of clustering other features of the insulin resistance/metabolic syndrome (2) and of predicting overall mortality (8). Recent experimental evidence suggests that adipocytes located in the abdominal region display distinct cellular features compared with adipocytes from other fat depots (5). Consequently, a specific dysfunction of the visceral adipocyte has been proposed as the pathophysiological basis for the negative consequences of abdominal obesity.

Although the epidemiological association between fat accumulation and excess risk of diabetes and of cardiovascular disease is striking, the biological mechanisms underlying the adverse impact of adipose tissue remain incompletely defined. Evidently, adipose tissue is not only responsible for storage of energy, but operates as a highly active and dynamic tissue. Adipocytes produce hormones and cytokines, collectively called adipokines, with pleiotropic effects on multiple tissues, leading to fine tuning of fuel utilization, energy homeostasis, and cardiovascular function. It should also be recognized that the functional attitude of visceral and subcutaneous adipocytes is programmed quite early during development and differentiation, due to inherent characteristics of the adipocyte precursors, multipotent cells that are resident in each fat depot and possess defined depot-specific genetic, biochemical, and metabolic features (3, 7, 9, 12, 15). Thus, the biological specificity of the distinct adipose tissue depots may reside in the different biological profile of the resident cells, including the adipocyte precursors.

On November 14 and 15, 2008, the University of Bari hosted the 3rd International Conference on “Molecular Basis of Metabolic Regulation”, an initiative in conjunction with the COST Programme of the European Science Foundation, specifically with the COST Action BM0602 entitled “Adipose Tissue: A Key for Prevention of the Metabolic Syndrome”. The goal of the Conference was to discuss recent experimental evidence on the physiology and pathophysiology of adipose tissue as a critical mediator of the development of metabolic abnormalities and enhanced cardiovascular risk. Specific topics of the Conference included the differentiation process determining the development of the adipose tissue; the molecular switches regulating adipocyte metabolism and the related signaling mechanisms, including the role of newly identified proteins involved in lipid vesicle turnover and fat oxidation; the biology of different fat depots; the fat-derived inflammatory molecules and cytokines contributing to the pathogenesis of insulin resistance, β-cell dysfunction, and cardiovascular damage; and the modulation of gene–environment interactions by the adipose tissue mass in type 2 diabetes. In this issue, a series of review articles originating from some of the presentations at the Conference address the modern view of the adipose organ as a key “transducer” of signals emanating from the genetic background and environment (i.e., changes in nutrient load and energy expenditure), that has the ability to variably affect various metabolic and cardiovascular outcomes, including insulin sensitivity, β-cell function, blood pressure levels, and atherogenesis, ultimately influencing morbidity for type 2 diabetes and cardiovascular disease, as well as long-term mortality (Fig. 1).
The review article by Cinti (4) discusses the functional properties of white and brown adipocytes, traditionally viewed as two completely distinct cell types, the former as an energy-storing cell and the latter as a heat-producing cell, and the anatomicatic properties that make it possible to identify them. However, the author proposes the novel concept that these different cell types are mixed together within the same adipose tissue in the various subcutaneous and visceral depots and that they are able to trans-differentiate reciprocally in order to meet different requests of energy partitioning or following physiological stimuli (e.g., cold vs. warm exposure and pregnancy/lactation), highlighting the important regulatory role of the sympathetic nervous system in this process. The concept that trans-differentiation is the main process explaining the adipose tissue plasticity in rodents is thus endorsed; the recent finding of the presence and localization of brown adipose tissue in humans (14) makes this concept particularly interesting.

In line with these views, the article by Vettor et al. (13) examines the development and metabolic role of the adipose tissue present within the skeletal muscle but outside of the myocellular fibers, the so-called “intermuscular adipose tissue (IMAT). The IMAT characteristically expands with aging and in the presence of metabolic and endocrine diseases such as obesity, type 2 diabetes, partial lipodystrophies, and acromegaly, and it is reduced by aerobic exercise. It is possible, therefore, that IMAT plays an important role in the pathogenesis of insulin resistance in skeletal muscle. The article discusses the interesting issue of the origin of IMAT from muscle satellite stem cells, which possesses the ability to differentiate into adipocytes instead of skeletal muscle fibers when specific conditions occur, as such as in the presence of high glucose concentrations (1).

The review article by Gustafson et al. (6) explores the relationship between dysregulated adipose tissue and cellular insulin resistance and describes the experimental evidence suggesting the hypothesis that activated preadipocytes, rather than macrophages, may account for the increased release of numerous molecules with great capacity to affect other cells and tissues, which include the ability of its resident cells to trans-differentiate or exchange functional phenotypes, the possibility to originate and expand in critical tissue sites from noncanonical precursors (e.g., IMAT from muscle satellite stem cells), and the secretion, even at the stage of adipocyte precursors, of numerous molecules with great capacity to affect other cells and tissues.

REFERENCES


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